

Table. PUFAs and CHD/CVD: Animal Studies

Author/ Year	De- sign Type	Class	Quality (+,-,Ø)	Purpose/ Population Sample Size	Regimen	Primary Outcome Measures Results	Author's Conclusions/ Reviewer's Comments (<i>Italicized</i>)
Rudel et al., 1997 (Hepatic origin of cholesteryl oleate in coronary artery atherosclero- sis in African green monkeys)	Non- ran- dom- ized trial	C	+	<p>Purpose: To discover correlation bet plasma lipoprotein chol, chol secretion by perfused liver and coronary artery atherosclerosis</p> <p>Sample: 44 male African green monkeys</p> <p>Inclusions: Adult male African green monkeys with equivalent TC and HDL to 8-wk diet</p> <p>Exclusions: None listed</p>	<p>Run-in Period: 8-wk challenge diet containing SFA and chol</p> <p>TX/Duration: 1) PUFA group: >70% linoleic acid 2) MUFA group: >70% oleic acid 3) SFA group: >40% palmitic acid</p> <p>60 mo</p> <p>No CNTL group</p> <p>Dose/Form: 1) PUFA group: linoleic- rich safflower oil 2) MUFA group: oleic-rich safflower oil 3) SFA composition not reported</p> <p>Dietary Intake During Study: Total fat (% TE): 35% in all groups SFA (% TE): not reported Chol: 0.8 mg/kcal Calories: not reported</p> <p>Dietary Intake</p>	<p>Outcome Measures: Liver conc of free chol, cholesteryl ester, TG, phospholipids FA conc Lipid and apolipoprotein accumulation Atherosclerosis</p> <p>Results: Liver free chol sig diff ($P<0.04$) among groups: MUFA (safflower oil): 4.53±0.7 mg/g wet wt SFA: 3.11±0.3 mg/g wet wt PUFA (safflower oil): 2.76±0.2 mg/g wet wt</p> <p>Liver cholesteryl ester conc sig diff ($P<0.0005$) among groups: MUFA (safflower oil): 8.46±1.3 mg/g wet wt SFA: 3.65±0.7 mg/g wet wt PUFA (safflower oil): 3.37±0.5 mg/g wet wt</p> <p>Liver TG NS diff among groups</p> <p>Liver phospholipids sig diff ($P<0.001$) among groups: SFA: 21.3±0.8 mg/g wet wt PUFA (safflower oil): 24.4±1.2 mg/g wet wt</p>	<p>Author's Conclusions: "In summary, the liver appears to be the primary source of the cholesteryl oleate that accumulates in plasma LDL particles. The cholesteryl oleate enrichment occurs as a result of the hepatic secretion of ACAT- derived cholesteryl oleate in apoB- containing lipoproteins. The increased secretion of cholesteryl oleate enriched lipoproteins by the liver was well correlated with the extent of coronary artery atherosclerosis in these African green monkeys"</p> <p>Reviewer's Comments: <i>None</i></p>

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					Assessment/Frequency: Not reported	<p>MUFA (safflower oil): 26.9±0.9 mg/g wet wt</p> <p>FA conc: Cholesteryl oleate highest in MUFA (safflower oil) group (75±2.8%; $P=0.0001$)</p> <p>Cholesteryl linoleate highest in PUFA (safflower oil) group (40±3.5%; $P=0.0001$)</p> <p>Cholesteryl palmitate highest in SFA group (12.6±0.7%; $P=0.0001$)</p> <p>Cholesteryl stearate highest in SFA group (7.9±0.6%; $P=0.0001$)</p> <p>Accumulation of perfusate lipids and apolipoprotein NS diff among groups</p> <p>Correlation bet liver chol conc and plasma apolipoprotein conc stat sig for PUFA (safflower oil) group ($r=0.57$, $P<0.05$) and SFA ($r=0.81$, $P<0.01$) and MUFA (safflower oil; $r=0.86$, $P<0.01$) groups</p> <p>Correlation bet liver perfusate cholesteryl ester accumulation</p>	

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						and coronary artery atherosclerosis stat sig for SFA ($r=0.87$, $P<0.01$), MUFA (safflower oil; $r=0.84$, $P<0.01$) and PUFA (safflower oil; $r=0.73$, $P<0.05$) groups	
Rudel et al., 1995(a) (Compared with dietary MUFA and SFA, PUFA protects African green monkeys from coronary artery atherosclerosis)	Non-randomized trial	C	+	Purpose: To assess whether substitution of MUFA or PUFA for SFA in diet limits coronary artery atherosclerosis Sample: 44 African green monkeys Inclusions: Feral adult male African green monkeys Exclusions: None listed	Run-in Period: Challenge diet high in SFA and chol until groups similar TC conc; followed by 10-wk washout TX/Duration: PERIOD 1 (start of study-42 mo): 1) PUFA diet with >70% linoleic acid 2) SFA diet with 40% palmitic acid 3) MUFA diet with >70% oleic acid 8-wk washout PERIOD 2 (42 mo-5 y): 1) PUFA diet with 100% linoleic acid 2) SFA diet with 100% palmitic acid 3) MUFA diet with 100% oleic acid No CNTL group	Outcome Measures: TC, HDL, LDL, TG Cholesteryl ester conc Apolipoprotein A1, A2, B, E Coronary artery intimal area Internal elastic lamina Lumen stenosis Results: % change in TC not reported TC sig incr SFA (palm oil) diet (422 ± 9 mg/dl) during period 2 compared to: MUFA (enriched safflower oil) diet: 313 ± 11 mg/dl ($P<0.03$) PUFA (safflower oil) diet: 276 ± 8 mg/dl ($P<0.002$) NS diff bet PUFA and MUFA diets NS diff in LDL bet diets % change in HDL not reported HDL in MUFA (enriched safflower oil) diet (87 ± 2 mg/dl) sig incr compared to: SFA (palm oil) diet: 75 ± 1	Author's Conclusions: "Dietary polyunsaturated fat appears to result in the least amount of coronary artery atherosclerosis because it prevents cholesteryl oleate accumulation in LDL and the coronary arteries in these primates" Reviewer's Comments: <i>Any diff >P=0.1 considered NS; extent of coronary artery atherosclerosis similar in SFA and MUFA groups and greater than PUFA group even in light of HDL levels</i>

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					<p>Dose/Form: 1) PUFA diet of safflower oil; >70% during period 1, 100% during period 2 2) SFA diet of palm oil; 40% during period 1, 100% during period 2 3) MUFA diet of enriched safflower oil; >70% during period 1, 100% during period 2</p> <p>Dietary Intake During Study: Total fat (% TE) for all groups: 35% SFA (% TE): not listed Chol for all groups: 0.8 mg/kcal Calories: 100 kcal/kg/d</p> <p>Dietary Intake Assessment/Frequency: Animals fed weighed portions 2x/d; raw carrots given 3x/wk as snack; bimonthly blood sampling</p>	<p>mg/dl ($P=0.06$) PUFA (safflower oil) diet: 48 ± 1 mg/dl ($P=0.0001$) HDL in PUFA (safflower oil) diet sig decr vs SFA (palm oil) group ($P=0.0008$)</p> <p>% change in TG not reported TG in PUFA (safflower oil) diet (15 ± 3 mg/dl) sig lower in period 2 compared to: SFA (palm oil) diet: 26 ± 4 mg/dl ($P<0.01$) MUFA (enriched safflower oil) diet: 24 ± 7 mg/dl ($P<0.01$)</p> <p>Cholesteryl ester conc NS diff bet diets</p> <p>% change in apolipoprotein A1 not reported Apolipoprotein in PUFA (safflower oil) diet (200 mg/dl) sig decr compared to: SFA (palm oil) diet: 261 mg/dl (no P reported) MUFA (enriched safflower oil) diet: 272 mg/dl (no P reported)</p> <p>Apolipoprotein A2 sig diff bet PUFA (safflower oil) (18 mg/dl) and MUFA (enriched safflower oil) (21 mg/dl) diets (no P reported)</p>	

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						<p>reported)</p> <p>Apolipoprotein B sig diff bet MUFA (enriched safflower oil) (114 mg/dl) and SFA (palm oil) (153 mg/dl) diets (no <i>P</i> reported)</p> <p>Apolipoprotein E sig incr SFA (palm oil) diet (8.1 mg/dL) vs MUFA (enriched safflower oil) or PUFA (safflower oil) diets (no absolute or <i>P</i> values reported)</p> <p>Coronary artery intimal area sig diff bet PUFA (safflower oil; 0.31 m²) and SFA (palm oil; 1.60 m²) diets (<i>P</i>=0.07)</p> <p>Sig diff bet PUFA (safflower oil) and MUFA (enriched safflower oil; 0.76 m²) diets (<i>P</i>=0.09)</p> <p>NS diff bet MUFA (enriched safflower oil) and SFA (palm oil) diets</p> <p>Internal elastic lamina sig smaller in PUFA (safflower oil; 0.97±0.1 mm²) diet than SFA (palm oil; <i>P</i>=0.005) or MUFA (enriched safflower oil) diet (<i>P</i>=0.05)</p> <p>Lumen stenosis sig diff bet SFA (palm oil) and PUFA (safflower</p>	

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						oil) diets ($P=0.05$)	
Rudel et al., 1995(b) (Dietary PUFA modifies LDL and reduces atherosclero- sis of nonhuman primates with high and low diet responsive- ness)	Non- ran- dom- ized trial	C	+	<p>Purpose: To identify whether beneficial effects of PUFA on lipoprotein metabolism seen in 2 primate species</p> <p>Sample: 54 male African green monkeys; 20 male cynomolgus monkeys</p> <p>Inclusions: Feral male African green monkeys and cynomolgus monkeys</p> <p>Exclusions: Monkeys with high BP, high glucose, abnormal blood urea nitrogen and high blood lipids</p>	<p>Run-in Period: None</p> <p>TX/Duration: CYNOMOLGUS MONKEY DIETS: 1) Low chol SFA diet (low SFA): approx 16% TE from SFA, 0.04 mg chol/kcal 2) Low chol PUFA diet (low PUFA): approx 28% TE from PUFA, 0.04 mg chol/kcal 3) High chol SFA diet (high SFA): approx 16% TE from SFA, 0.45 mg chol/kcal 4) High chol PUFA diet (high PUFA): approx 28% TE from PUFA, 0.45 mg chol/kcal</p> <p>3 y</p> <p>AFRICAN GREEN MONKEY DIETS: 1) Low chol SFA diet (low SFA): approx 16% TE from SFA, 0.03 mg chol/kcal 2) Low chol PUFA diet</p>	<p>Outcome Measures: TC, LDL, LDL particle size, HDL, TG Cholesteryl esters Apolipoprotein A1, B Coronary artery atherosclerosis</p> <p>Results: % change in TC not reported TC sig incr with dietary chol ($P<0.0001$) in both species TC NS diff bet species TC sig decr in both species when PUFA (safflower oil) vs SFA (lard) fed ($P\leq 0.05$)</p> <p>% change in LDL not reported LDL sig incr in both species when high chol diets fed ($P<0.05$) Trend for lower LDL with PUFA (safflower oil) diets NS</p> <p>LDL particles sig larger in cynomolgus monkeys than African green monkeys ($P<0.0001$) Incr dietary chol assoc with sig incr in LDL particle size in both species ($P<0.001$) LDL particles larger in cynomolgus monkeys ($P=0.05$)</p>	<p>Author's Conclusions: "Therefore, in these nonhuman primate species, the extent of coronary artery atherosclerosis was highly related to LDL composition and concentration....This outcome suggests that information about LDL composition may be more important for understanding the pathogenesis of atherosclerosis than previously suspected"</p> <p>Reviewer's Comments: <i>None</i></p>

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					<p>(low PUFA): approx 19% TE from PUFA, 0.03 mg chol/kcal</p> <p>3) High chol SFA diet (high SFA): approx 16% TE from SFA, 0.8 mg chol/kcal</p> <p>4) High chol PUFA diet (high PUFA): approx 19% TE from PUFA, 0.8 mg chol/kcal</p> <p>5 y</p> <p>Dose/Form: CYNOMOLGUS MONKEYS:</p> <p>1) SFA diets: lard; approx 16% TE</p> <p>2) PUFA diets: safflower oil; approx 28% TE</p> <p>AFRICAN GREEN MONKEYS:</p> <p>1) SFA diets: lard; approx 16% TE</p> <p>2) PUFA diets: safflower oil; approx 19% TE</p> <p>Dietary Intake During Study: Total fat (% TE): 40% for both groups of monkeys</p> <p>SFA (% TE)</p>	<p>fed PUFA (safflower oil)</p> <p>% change in HDL not reported HDL sig decr in all monkeys on PUFA (safflower oil) diets compared to SFA (lard) diets ($P<0.05$)</p> <p>% change in TG not reported TG sig decr in both species fed PUFA (safflower oil) diets vs SFA (lard) diets ($P<0.005$)</p> <p>Cholesteryl oleate in cynomolgus monkeys sig incr ($P<0.001$) vs African green monkeys</p> <p>Cholesteryl linoleate sig incr in PUFA (safflower oil) diet ($P<0.0001$) vs SFA (lard) diet in both species</p> <p>Apolipoprotein A1 sig incr in cynomolgus monkeys fed high chol diets ($P<0.05$); NS diff due to diet in African green monkeys</p> <p>Apolipoprotein B sig decr in cynomolgus monkeys fed PUFA (safflower oil) vs SFA (lard) diets ($P<0.05$); sig incr in African green monkeys fed high chol vs low chol diets ($P<0.05$)</p>	

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					<p>Cynomolgus: 16% African green monkey: not reported Chol (mg/kcal) Cynomolgus: Low chol diets: 0.04 High chol diets: 0.45 African green monkeys: Low chol diets: 0.03 High chol diets: 0.8 Calories: not reported</p> <p>Dietary Intake Assessment/Frequency: Details of dietary assessment not reported; animals individually housed; blood taken periodically</p>	<p>Cynomolgus monkeys sig incr atherosclerosis than African green monkeys ($P<0.0001$)</p> <p>In both species high chol diets sig incr coronary artery atherosclerosis than low chol diets ($P<0.01$) High chol PUFA (safflower oil) diet sig decr atherosclerosis vs high chol SFA (lard) diet ($P<0.01$)</p> <p>Coronary artery atherosclerosis highly related to LDL cholesteryl oleate ($r=0.8$, $P<0.001$). Relation bet mean coronary artery atherosclerosis and mean LDL for all 8 groups sig ($r=0.9$, $P<0.0001$)</p>	
Wolfe et al., 1994	Non- ran- dom- ized trial	C	+	<p>Purpose: To evaluate long-term effects of dietary PUFA on coronary artery atherosclerosis in pediatric-aged African green monkeys</p> <p>Sample: 108 juvenile African green monkeys</p>	<p>Run-in Period: Mothers consumed same diet as progeny before and during pregnancy and lactation</p> <p>TX/Duration: Monkeys given PUFA diet or SFA diet until death at age 16 mo, 32 mo or 60 mo</p>	<p>Outcome Measures: TC, LDL, VLDL, ILDL, HDL Apolipoprotein A1, B Coronary artery atherosclerosis (Coronary artery intimal area) Atherosclerosis severity (maximal intimal thickness) Abdominal aorta atherosclerosis Atherosclerosis in thoracic aorta, carotid artery bifurcations, common carotid</p>	<p>Author's Conclusions: "The reduction in coronary artery atherosclerosis induced by dietary polyunsaturated fat in the juvenile African green monkey appears to have direct implications for diet- induced reductions in</p>

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				<p>Inclusions: Male and female juvenile African green monkeys</p> <p>Exclusions: None listed</p>	<p>Dose/Form: 1) PUFA diet: approx 20% kcal from n-6 PUFA 2) SFA diet: approx 5.5% kcal from n-6 PUFA</p> <p>Details of fat/oil composition not reported</p> <p>Dietary Intake During Study: Total fat (% TE) PUFA: 40 SFA: 40 SFA (% TE) PUFA: not reported SFA: not reported Chol PUFA: 0.8 mg/kcal SFA: 0.8 mg/kcal Calories: not reported</p> <p>Dietary Intake Assessment/Frequency: Monkeys group housed and then individually caged once sexual maturity reached; no other feeding details provided</p>	<p>arteries</p> <p>Results: Total or % change in lipids not reported</p> <p>NS diff in TC bet groups; NS trend for lower TC in PUFA groups</p> <p>NS diff in LDL bet groups</p> <p>HDL sig decr ($P=0.0005$) in PUFA vs SFA groups</p> <p>Apolipoprotein A1 NS diff bet groups</p> <p>Apolipoprotein B sig incr in males vs females ($P=0.05$) on both diets</p> <p>Atherosclerosis had sig ($P=0.02$) age-related incr bet 32 and 60 mo</p> <p>PUFA groups sig less intimal area than SFA groups ($P=0.01$)</p> <p>Intimal area sig incr in males at age 60 mo compared to females ($P=0.03$) regardless of group</p>	<p>the risk of CHD in children"</p> <p>Reviewer's Comments: <i>FA conc of mothers' milk reflected their diets; diets used in study designed to mimic dietary fat in Western diet; chol in diet from dried egg yolk</i></p>

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						<p>Maximal intimal thickness incr sig ($P=0.007$) with age in both groups; PUFA groups sig less maximal intimal thickness ($P=0.007$) than SFA groups.</p> <p>PUFA groups sig smaller lesions than SFA groups ($P=0.007$).</p> <p>Abdominal aorta atherosclerosis incr sig bet 32 and 60 mo ($P=0.0001$); diff bet diet groups NS</p> <p>SFA group sig incr free chol in abdominal aorta than PUFA group ($P=0.02$)</p> <p>NS diff in intimal areas bet groups for thoracic aorta, carotid artery bifurcations or common carotid arteries; 60-mo-old male monkeys sig incr atherosclerosis in each of these arteries vs females ($P\leq 0.04$)</p>	

APPENDIXQ2PUFAAnimalTable